

I

wherein the dashed lines represent optional double bonds;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E, or D is CH and is single bonded to E;

F is [oxygen, sulfur,] CHR^4 or NR^4 when it is single bonded to E; provided that at least one of D and E is nitrogen or F is NR^4 , and provided that only one of D and E is nitrogen, and D and E are not nitrogen when F is NR^4 ;

G, when single bonded to E, is hydrogen, C_1 - C_4 alkyl, $-S(C_1$ - C_4 alkyl), $-O(C_1$ - C_4 alkyl), NH_2 , $-NH(C_1$ - C_4 alkyl) or $-N(C_1$ - C_2 alkyl)(C_1 - C_4 alkyl), wherein each of the C_1 - C_4 alkyl groups of G may optionally be substituted with one hydroxy, $-O(C_1$ - C_2 alkyl) or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

R^1 is hydrogen, C_1 - C_6 alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, CF_3 , $-C(=O)O$ -(C_1 - C_4)alkyl, $-OC(=O)(C_1$ - C_4 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-NHCO(C_1$ - C_4 alkyl), $-COOH$, $-COO(C_1$ - C_4 alkyl), $-CONH(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_4 alkyl), $-CN$, $-NO_2$, $-SO(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2NH(C_1$ - C_4 alkyl) and $-SO_2N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), wherein a carbon-carbon single bond of each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond; R^2 is C_1 - C_{12} alkyl wherein one carbon-carbon single bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said

alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or R^2 is aryl or $(C_1-C_4 \text{ alkylene})\text{aryl}$, wherein said aryl and the aryl moiety of said $(C_1-C_4 \text{ alkylene})\text{aryl}$ is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R^2 is C_3-C_8 cycloalkyl or $(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$, wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(C_1-C_6 \text{ alkylene})(C_3-C_8 \text{ cycloalkyl})$ may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1-C_4 alkyl, or with one substituent selected from bromo, iodo, C_1-C_6 alkoxy, $-OC(=O)(C_1-C_6 \text{ alkyl})$, $-OC(=O)N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_6 \text{ alkyl})$, amino, $-NH(C_1-C_2 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})-CO-(C_1-C_4 \text{ alkyl})$, $-NHCO(C_1-C_4 \text{ alkyl})$, $-COOH$, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-SH$, $-CN$, $-NO_2$, $-SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$;

$-NR^1R^2$ or $-CR^1R^2R^{10}$ may form a saturated 3 to 8 membered ring that, in the case of $-CR^1R^2R^{10}$, is carbocyclic, and that, in the case of $-NR^1R^2$, contains a single heteroatom, nitrogen, which ring may optionally contain from one to three double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen, C_1-C_4 alkyl, benzyl or C_1-C_4 alkanoyl;

R^3 is hydrogen, C_1-C_4 alkyl, $-O(C_1-C_4 \text{ alkyl})$, chloro, fluoro, bromo, iodo, $-CN$, $-S(C_1-C_4 \text{ alkyl})$ or $-SO_2(C_1-C_4 \text{ alkyl})$ wherein each of the $(C_1-C_4 \text{ alkyl})$ moieties in the foregoing R^3 groups may optionally be substituted with one substituent R^9 selected from hydroxy, fluoro and $(C_1-C_2 \text{ alkoxy})$;

each R^4 is, independently, hydrogen, $(C_1-C_6 \text{ alkyl})$, fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, $-O(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-CO(C_1-C_4 \text{ alkyl})$, $-C(=O)H$ or $-C(=O)O(C_1-C_4 \text{ alkyl})$, wherein one or two of the carbon-carbon single bonds in each of the $(C_1-C_6 \text{ alkyl})$ and $(C_1-C_4 \text{ alkyl})$ moieties in the foregoing R^4 groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of these moieties may optionally be substituted

with one or two substituents independently selected from hydroxy, amino, C₁-C₃ alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH₃, fluoro, chloro, C₁-C₃ alkylthio, -CN, -COOH, -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl) and -NO₂;

R⁵ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C₃-C₈ cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ⁴ wherein Z⁴ is hydrogen, C₁-C₄ alkyl or benzyl; and wherein each of the foregoing R⁵ groups is substituted with from one to four substituents R¹² wherein one to three of said substituents may be selected, independently, from chloro, C₁-C₆ alkyl and -O(C₁-C₆ alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF₃, -NO₂, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₆ alkyl), -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl), -COOH, -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl, and wherein a carbon-carbon single bond of each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups having between two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond]; and furthermore wherein when R⁵ is phenyl or pyridyl substituted with two or three substituents, said substituents can further be selected from (C₁-C₄ alkyl)O(C₁-C₄ alkyl), OCF₃, and fluoro, and one carbon-carbon single bond of each (C₁-C₄) alkyl group of said substituents having between two and four carbon atoms may be optionally replaced with a carbon-carbon double or triple bond; or R⁵ is pyrimidyl substituted by two or three substituents independently selected from C₁-C₄ alkyl, -O(C₁-C₄ alkyl), CF₃, OCF₃, -CHO, (C₁-C₄ alkyl)-OH, CN, Cl, F, Br, I and NO₂, wherein a carbon-carbon single bond of said (C₁-C₄) alkyl groups having between two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond;

R⁷ is hydrogen, C₁-C₄ alkyl, halo, cyano, hydroxy, -O(C₁-C₄ alkyl) -C(=O)(C₁-C₄ alkyl), -C(=O)O(C₁-C₄alkyl), -OCF₃, -CF₃, -CH₂OH, -CH₂O(C₁-C₄ alkyl);

R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹ is hydrogen or C₁-C₄ alkyl; and

with the proviso that: (a) when R^4 is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

Z is NH, oxygen, sulfur, $-N(C_1-C_4 \text{ alkyl})$, $-NC(=O)(C_1-C_2 \text{ alkyl})$, $NC(=O)O(C_1-C_2 \text{ alkyl})$ or $CR^{13}R^{14}$ wherein R^{13} and R^{14} are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R^{13} and R^{14} can be cyano;

or a pharmaceutically acceptable salt of such compound.

20. (Twice amended) A pharmaceutical composition for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF; or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, [fatigue syndrome,] stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, ulcers, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, [obesity,] head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, psychosocial dwarfism, and hypoglycemia in a mammal, comprising an amount of a compound according to claim 18 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.

21. (Twice amended) A method for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression,

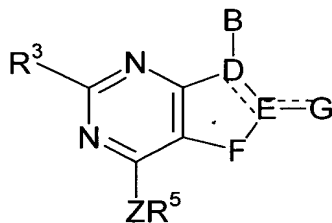
recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, [fatigue syndrome,] stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, [obesity,] head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, ulcers, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, psychosocial dwarfism, and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim 18, that is effective in treating such disorder.

23. (Amended) A pharmaceutical composition for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF; or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, [fatigue syndrome,] stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, ulcers, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, [obesity,] head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, psychosocial dwarfism, and hypoglycemia in a mammal, comprising an amount of a compound according to claim [22] 25 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.

24. (Amended) A method for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, [fatigue syndrome,] stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, [obesity,] head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, ulcers, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, psychosocial dwarfism, and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim [22] 25, that is effective in treating such disorder.

Please add the following claim 25:

--25. A compound of the formula



wherein the dashed lines represent optional double bonds;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E, or D is CH and is single bonded to E;

F is oxygen, sulfur, CHR^4 or NR^4 when it is single bonded to E; provided that at least one of D and E is nitrogen or F is NR^4 , and provided that only one of D and E is nitrogen, and D and E are not nitrogen when F is NR^4 ;

G, when single bonded to E, is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, $\text{-S(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-O(C}_1\text{-C}_4\text{ alkyl)}$, NH_2 , $\text{-NH(C}_1\text{-C}_4\text{ alkyl)}$ or $\text{-N(C}_1\text{-C}_2\text{ alkyl)(C}_1\text{-C}_4\text{ alkyl)}$, wherein each of the $\text{C}_1\text{-C}_4$ alkyl groups of G may optionally be substituted with one hydroxy, $\text{-O(C}_1\text{-C}_2\text{ alkyl)}$ or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

R^1 is hydrogen, $\text{C}_1\text{-C}_6$ alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, $\text{C}_1\text{-C}_4$ alkoxy, CF_3 , $\text{-C(=O)O(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-OC(=O)(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-OC(=O)N(C}_1\text{-C}_4\text{ alkyl)(C}_1\text{-C}_2\text{ alkyl)}$, $\text{-NHCO(C}_1\text{-C}_4\text{ alkyl)}$, -COOH , $\text{-COO(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-CONH(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-CON(C}_1\text{-C}_4\text{ alkyl)(C}_1\text{-C}_2\text{ alkyl)}$, $\text{-S(C}_1\text{-C}_4\text{ alkyl)}$, -CN , -NO_2 , $\text{-SO(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-SO}_2\text{(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-SO}_2\text{NH(C}_1\text{-C}_4\text{ alkyl)}$ and $\text{-SO}_2\text{N(C}_1\text{-C}_4\text{ alkyl)(C}_1\text{-C}_2\text{ alkyl)}$, wherein a carbon-carbon single bond of each of the $\text{C}_1\text{-C}_4$ alkyl groups in the foregoing R^1 groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the $\text{C}_1\text{-C}_4$ alkyl groups in the foregoing R^1 groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond; R^2 is $\text{C}_1\text{-C}_{12}$ alkyl wherein one carbon-carbon single bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or R^2 is aryl or $\text{(C}_1\text{-C}_4\text{ alkylene)aryl}$, wherein said aryl and the aryl moiety of said $\text{(C}_1\text{-C}_4\text{ alkylene)aryl}$ is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R^2 is $\text{C}_3\text{-C}_8$ cycloalkyl or $\text{(C}_1\text{-C}_6\text{ alkylene)(C}_3\text{-C}_8\text{ cycloalkyl)}$, wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $\text{(C}_1\text{-C}_6\text{ alkylene)(C}_3\text{-C}_8\text{ cycloalkyl)}$ may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, $\text{C}_1\text{-C}_4$ alkyl, benzyl and $\text{C}_1\text{-C}_4$ alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and $\text{C}_1\text{-C}_4$ alkyl, or with one substituent selected from bromo, iodo, $\text{C}_1\text{-C}_6$ alkoxy, $\text{-OC(=O)(C}_1\text{-C}_6\text{ alkyl)}$, $\text{-OC(=O)N(C}_1\text{-C}_4$

alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), amino, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)-CO-(C₁-C₄ alkyl), -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SH, -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl);

-NR¹R² or -CR¹R²R¹⁰ may form a saturated 3 to 8 membered ring that, in the case of -CR¹R²R¹⁰, is carbocyclic, and that, in the case of -NR¹R², contains a single heteroatom, nitrogen, which ring may optionally contain from one to three double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by NZ³ wherein Z³ is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl;

R³ is hydrogen, C₁-C₄ alkyl, -O(C₁-C₄ alkyl), chloro, fluoro, bromo, iodo, -CN, -S(C₁-C₄ alkyl) or -SO₂(C₁-C₄ alkyl) wherein each of the (C₁-C₄ alkyl) moieties in the foregoing R³ groups may optionally be substituted with one substituent R⁹ selected from hydroxy, fluoro and (C₁-C₂ alkoxy);

each R⁴ is, independently, hydrogen, (C₁-C₆ alkyl), fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, -O(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ alkyl), -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄)alkyl, -CO(C₁-C₄ alkyl), -C(=O)H or -C(=O)O(C₁-C₄alkyl), wherein one or two of the carbon-carbon single bonds in each of the (C₁-C₆ alkyl) and (C₁-C₄ alkyl) moieties in the foregoing R⁴ groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of these moieties may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C₁-C₃ alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH₃, fluoro, chloro, C₁-C₃ alkylthio, -CN, -COOH, -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl) and -NO₂;

R⁵ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C₃-C₈ cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ⁴ wherein Z⁴ is hydrogen, C₁-C₄ alkyl or benzyl; and wherein each of the foregoing R⁵ groups is substituted with from one to four substituents R¹² wherein one to three of said substituents may be selected, independently, from chloro, C₁-C₆ alkyl and -O(C₁-C₆ alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF₃, -NO₂, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₆ alkyl), -C(=O)O(C₁-C₄ alkyl),

-C(=O)(C₁-C₄ alkyl), -COOH, -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R⁷ is hydrogen, C₁-C₄ alkyl, halo, cyano, hydroxy, -O(C₁-C₄ alkyl) -C(=O)(C₁-C₄ alkyl), -C(=O)O(C₁-C₄alkyl), -OCF₃, -CF₃, -CH₂OH, -CH₂O(C₁-C₄ alkyl);

R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹ is hydrogen or C₁-C₄ alkyl; and

with the proviso that: (a) when R⁴ is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

Z is NH, oxygen, sulfur, -N(C₁-C₄ alkyl), -NC(=O)(C₁-C₂ alkyl), NC(=O)O(C₁-C₂alkyl) or CR¹³R¹⁴ wherein R¹³ and R¹⁴ are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R¹³ and R¹⁴ can be cyano;

or a pharmaceutically acceptable salt of such compound.---

REMARKS

This communication is submitted in response to the March 26, 1999 Office Action. Upon entry of the above amendments, claims 2-4, 8-10, 12-14, 18, and 20, 21, 23, 24, and 25 will be pending in this application.

Applicant maintains that support for the above amendments to the claims can be found in the originally-filed specification. The particular support for each amendment is discussed in detail below, where each amendment and the reasons therefor are discussed in turn. Accordingly, applicant maintains that the amendments do not raise an issue of new matter.

Certain references mentioned in the following remarks are also listed on the attached form in conformance with Form PTO-FB-A820. It is requested that the Examiner initial the attached form at the appropriate locations after review and consideration of each reference so that these references can be made of record.

In the March 26, 1999 Office Action, the Examiner maintained rejection of claims under 35 USC 112, first and second paragraphs, on the grounds that the claim language "a disorder the treatment of which can be effected or facilitated by antagonizing CRF" is allegedly vague. It is

EXPRESS MAIL NO. EL163959074VS